## REMARKS

Reconsideration of the instant application is respectfully requested in view of the amendments above and the following remarks.

Claims 1, 87, 90 and 98 have been amended. Previously withdrawn claims have been cancelled without prejudice. Claims 1, 10, 14, 24, 25, and 86, 87, and 89-98 are currently under consideration.

The support for the amendments to claim 1 is found at least on page 30 of the original application (siRNAs directed to portion 945-965 within ataxin mRNA, which is SEQ ID NO: 1). The support for the amendment to claim 90 is found at least in previously presented claim 98. The support for the amendment to claim 98 is found at least on pages 14 and 30 of the originally filed application. Accordingly, no new matter has been introduced with this response.

### SUMMARY OF THE INVENTION

Applicant's invention is directed to *inter alia* a medical system for treating a spinocerebellar ataxia type 1 in a human live patient comprising: (a) an intracranial access device; (b) a mapping means for locating a predetermined intraparenchymal location in the brain of the patient, said location comprising neurons natively expressing a gene encoding an ataxin-1 protein; (c) a deliverable amount of a small interfering RNA capable of reducing the amount of ataxin-1 protein produced in said neurons, or a vector encoding said small interfering RNA, wherein said small interfering RNA has a length of between about 15 and about 30 nucleotides; and (d) a delivery means for delivering said small interfering RNA or vector encoding said small interfering RNA to said location of the brain of said patient from said intracranial access device through a stereotactically implanted catheter, said catheter comprising a radiographic marker, wherein said small interfering RNA hybridizes to a sequence identical to SEQ ID NO: 1 within the ataxin-1 mRNA.

In another aspect, the invention provides a medical system for treating spinocerebellar ataxia type 1 in a human patient comprising: (a) an intracranial access device comprising a radiographic marker; (b) a mapping means for locating a predetermined location in the brain of the patient, said location comprising cells natively expressing a gene encoding an ataxin-1 protein; (c) a deliverable amount of a small interfering RNA capable of reducing the amount of ataxin-1 protein produced in said cells or a vector encoding said small interfering RNA, said small interfering RNA comprising any one of SEQ ID Nos: 1 and 2; and (d) a delivery means for

delivering said small interfering RNA or vector encoding said small interfering RNA to said location of the brain of said patient from said intracranial access device through a stereotactically implanted catheter.

The pending claims rather than relying on pre- or post- surgical mapping or imaging techniques of a patient's brain, employs such imaging procedures as guided stereotactical and triangulation techniques *during the actual brain surgery* to enhance delivery of siRNA to the locations of interest.

## AMENDMENTS TO THE SPECIFICATION

The Examiner objected to the specification alleging that the material incorporated with the previous amendment constitutes new matter. Applicant respectfully disagrees with this characterization and maintains that the previous amendment did not constitute new matter. Pursuant to 37 CFR § 1.57, incorporated information from another U.S. patent application is as much a part of the application as filed as if the text was repeated in the application. Therefore, such information should be treated as part of the text of the application as originally filed. Replacing the identified material incorporated by reference with the actual text is not new matter. (see MPEP § 2163.07(b)).

Nevertheless, Applicant amended the specification to remove Fig. 7, its description in the "Brief Description of the Drawings." Applicant also amended section "Devices" to remove the previously introduced quotation from U.S. Application 09/864,646. Accordingly, Applicant respectfully requests the withdrawal of the objection.

## CLAIM OBJECTIONS

The Examiner objected to claim 1 asserting that the recitation "comprising material which does not interfere with intra-operative brain imaging" is unclear. Specifically, the Examiner is questioning whether this recitation relates to the catheter, delivery means, siRNA, or any other part of the system. Claim 1 has been amended to clarify that the recitation at issue relates to the catheter. Thus, the objection to claim 1 should be withdrawn.

The Examiner also objected to claim 87 and suggested replacing "encoding for" with "encoding." Applicants thank the Examiner for the helpful suggestion. Claim 87 has been amended accordingly. Thus, the objection to claim 87 should be withdrawn.

## OBJECTION TO SPECIFICATION

The Examiner objected to the instant specification alleging that the added text constitutes impermissible addition of new matter. Applicants respectfully disagree. The added text is copied from the patent documents referenced in the specification and incorporated into the specification. Contrary to the Examiner's position, the added text is not taken out of context and does not violate the letter and the spirit of the rule against addition of new matter.

Nevertheless, Applicant amended the specification to comply with the Examiner's suggestion on page 5 of the Office Action. Applicant also respectfully notes that the patents and patent applications referenced in the instant specification (particularly, U.S. Application SN 09/872,698) comply with 37 CFR 1.57 and urge the Examiner to give full weight to these documents. Pursuant to 37 CFR § 1.57, incorporated information from another U.S. patent application is as much a part of the application as filed as if the text was repeated in the application. Therefore, such information should be treated as part of the text of the application as originally filed.

## REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

The Examiner rejected claims 1 and 90 (and their respective dependent claims) alleging that the language "patient-specific intraoperative mapping means" is indefinite. Applicant respectfully disagrees with the Examiner and notes that this recitation is definite considering the disclosure of the instant application and the patent documents referred to in the section "Devices" of the application as filed.

Nevertheless, in the interest of the expedited prosecution, Applicant removed this limitation from claim 1 and 90. Accordingly, Applicant respectfully requests the Examiner to withdraw this ground for rejection.

## REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (WRITTEN DESCRIPTION)

The Examiner rejected claims 1 and 90 (and their respective dependent claims) alleging that the language "patient-specific intraoperative mapping means for locating a predetermined location in the brain" lacks adequate written description. Applicants respectfully traverse.

A person of ordinary skill in the art is expected to know that imaging systems encompassed by the claims of the instant invention (such as, by way of example only, the PoleStar® iMRI Navigation Suite or StealthStation® manufactured and sold by Medtronic, Inc.

and noted in the response of September 27, 2008) exist and are commercially available. Accordingly, it follows that a person of the ordinary skill in the art would be on notice that the inventor, an employee of Medtronic, Inc., was in possession of such a system providing intra-operative patient-specific mapping means, such systems being manufactured and sold by Medtronic, Inc. since before March, 2001 (see Form 10-Q filed by Medtronic, Inc., for the period ending January 26, 2001, page 13, paragraph 6 "After quarter end, the Company announced the commercial launch of the StealthStation® TREON™ Treatment Guidance System, a product that will further improve accuracy and precision during brain and spinal surgery."),.

Nevertheless, without agreeing with the Examiner and solely for the purpose of expediting the prosecution of the instant application, claims 1 and 90, have been amended. In their current form, these claims do not have the recitation "patient-specific intraoperative."

Further, with regards to the mapping means, Applicant respectfully notes that the section "Devices" provides sufficient examples to a person of skill in the art to identify the meaning of "mapping means." Specifically and without limitations, Applicant refers to the following quote from U.S. Application 09/864,646 (paragraphs 0029-0032):

> [0029] FIG. 4 depicts an alternate preferred embodiment of the distal end 22 of the catheter 16, wherein a radiographic marker 46 is coupled to the tip 24. The radiographic marker 46 renders at least a portion of the tip 24 opaque to x-rays, enabling the tip 24 to be observed during fluoroscopy or via x-ray to facilitate placement of the distal end 22 and the tip 24. In a preferred embodiment, the radiographic marker 46 comprises a semispherical portion 48 that has a cylindrical nipple 50 emanating away therefrom. The semispherical portion 48 provides a rounded profile for minimizing tissue disruption during insertion. The cylindrical nipple 50 is sized to fit snugly within the lumen 45 and be held in place via a suitable biocompatible adhesive, such as a biocompatible medical silicone adhesive or a medical urethane adhesive. In a preferred embodiment, the radiographic marker 46 comprises tantalum powder dispersed in a matrix composed of a biocompatible adhesive, such as the ones discussed above. The preferred ratio of tantalum to adhesive is 3 to 2. Ordinarily, the radiographic marker 46 will be premolded prior to insertion into the lumen 45. After the radiographic marker 46 has been inserted into the lumen 45, a thin coating of the same biocompatible adhesive is preferably applied to the exterior of the semispherical portion 48. Other materials may also be suitable for the radiographic marker 46, such as barium or platinum materials.
>
> [0030] Alternatively, the radiographic marker 46 may be composed of a material that is compatible to nuclear magnetic resonance imaging (MRI) to enable the tip 24 to be detected during an MRI scan. A preferred material for the radiographic marker 46 in an MRI context is platinum, though barium, tantalum, and similar

materials are also suitable. Regardless of whether radiography or MRI is being utilized, the goal of providing a radiographic marker 46 is to enable the operator to accurately detect the precise location of the tip 24 to facilitate placement and later verification of the integrity and position of the catheter system 10.

[0031] Alternatively, the radiographic marker 46 may be composed of a material that has sufficient radio density for visualization during radiologic procedures, but in powdered form that is dispersed in the catheter tip 24 at the time the catheter tip 24 is molded.

[0032] The following example illustrates the customization feature of the catheter system 10. Assume, for the purposes of this illustration, that in the medical application depicted in FIGS. 1 and 2, the patient is suffering from Parkinson's disease and it is desired to place the catheter tip 24 in the putamen 26 of the brain 12 to deliver GDNF in a dosage of approximately 1.0 μl/h. As an initial step, the structural size of the putamen 26 can be determined by MRI. Once the structural size of the putamen 26 is determined, the physician can stimulate the tubular portion 38 to expand using the techniques discussed above and, by hand, slide the catheter tip 24 relative to the tubular portion 38 to achieve a length X that will provide maximal diffusion of the agent throughout the putamen 26 for accessing the different dopaminergic pathways. The distal end 22 and the catheter tip 24 are then positioned using known stereotactic techniques and the remainder of the catheter system 10 is placed as discussed above.

Applicant respectfully submits that this information provides sufficient evidence for the suitable mapping means such as, for example, MRI, stereotactic technique, X-ray, and fluoroscopy.

Application 09/864,646 is a U.S. Patent application which itself does not refer to another document for the necessary disclosure. Accordingly, this application complies with 37 C.F.R. § 1.57 and therefore, constitutes the part of the instant application, which can be used to find support for the disputed term.

For these reasons, Applicant respectfully requests withdrawal of the instant rejection ground.

**REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH (NEW MATTER)**

The Examiner rejected claims 1 and 90 (and their respective dependent claims) alleging that the language "patient-specific intraoperative" and "material that does not interfere with intraoperative brain imaging" constitutes new matter. With regard to the "patient specific intraoperative," Applicant respectfully notes that claims 1 and 90, as submitted with this Amendment, do not have this recitation.

With regard to the "material which does not interfere with intraoperative brain imaging," Applicant respectfully refers the Examiner at least to U.S. Application 09/864,646 (paragraphs 0029-0032) quoted above. Multiple radiographic markers are disclosed in that quote. None of these markers interferes with the complementary method of intraoperative brain imaging. Accordingly, a person of ordinary skill in the art would recognize that the radiographic marker does not interfere with the complementary imaging system. Nevertheless, claims 1 and 90 have been amended to replace the disputed term with "radiographic marker." The support for the term "radiographic marker" is found at least in paragraphs 0029-0032 of U.S. Application 09/864,646.

As discussed above, U.S. Application 09/864,646 complies with 37 CFR § 1.57 and therefore comprises an integral part of the instant specification. Since the proper support is present at least in the '946 application, Applicant respectfully requests the Examiner to withdrawn the instant rejection ground.

**PROVISIONAL OBVIOUSNESS-TYPE DOUBLE PATENTING REJECTIONS**

The Examiner rejected claims 1, 10, 14, and 25 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims of Application 10/962,372 in view of Elsberry et al. (US 6,042,579, "Elsberry") and Cummings et al., *Phil. Trans. R. Soc. Lond. B* 354: 1079-1081 (1999) ("Cummings"). Applicant respectfully submits that the claims of '372 application in combination with Elsberry and Cummings do not disclose or suggest a siRNA which hybridizes to a portion of ataxin-1 mRNA, said portion being identical to SEQ ID NO" 1.

Accordingly, Applicants respectfully request withdrawal of this provisional rejection.

**REJECTION ON THE BASIS OF 35 U.S.C. §103**

The Examiner has rejected claims 1, 10, 14, 24, 25, and 85-97 under 35 U.S.C. § 103 as being allegedly unpatentable over Elsberry in view of Davidson (US 2004/0023390) and Cummings. Applicant respectfully traverses.

Independent clams 1 and 90 are drawn to siRNAs which hybridize to a portion of ataxin 1 mRNA, which portion is identical to SEQ ID NO: 1. None of the prior art references, whether individually or in combination disclose or suggest this feature. Accordingly, Applicant respectfully maintains that claims 1 and 90 are not obvious in view of the references cited by the Examiner. All other claims depend either from claim 1 or claim 90, thus incorporating all

limitations of their respective independent claim. Since claims 1 and 90 are not obvious, the other claims under consideration are also not obvious.

Accordingly, Applicants respectfully request the Examiner to withdraw the instant ground for rejection.

## CONCLUSION

In view of the remarks above, Applicant submits that the pending claims are valid and favorable reconsideration and allowance are earnestly solicited. If, however, for any reason the Examiner does not believe that such action can be taken at this time, it is respectfully requested that the Examiner telephone Applicant's attorney at (609) 844-3020 to discuss any additional rejections. The USPTO is authorized to charge Deposit Account No. 50-1943 for any charges in connection with this matter.

Date: December 10, 2008

Respectfully submitted,

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